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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,408	05/17/2005	Thomas P. Quinn	UVMO:023US/10412756	2719

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,408	QUINN ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/09/2008 has been entered.

Claims 1-20 are pending.

Request for Rejoinder:

The restriction requirement between groups I and II, set forth in the Office communication mailed out 4/24/2007, is withdrawn.

Claims 1-20 are examined on the merits.

Claim Rejections/Objections Withdrawn:

Claim Rejections - 35 USC § 112

The rejection of claims 1-4 and 7-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants' amendment to claim 1, adding the limitation that the peptide binds to the extracellular domain of ErbB2.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 14-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because "said cancer cell" lacks antecedent basis.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for targeting an agent to a cell expressing ErbB-2 comprising bringing a cancer cell into contact with a peptide-agent complex, wherein the peptide of the peptide-agent complex comprises the sequence of KCCYSL (SEQ ID NO: 1), and wherein the agent is a diagnostic agent, does not reasonably provide enablement for methods wherein the agent is any therapeutic agent, or a nucleic acid construct. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 5-20 are drawn to methods comprising targeting an agent to a cell expressing ErbB-2 comprising bringing the cell into contact with a peptide-agent complex, where the agent is a nucleic acid construct, and where the peptide comprises the sequence KCCYSL (SEQ ID NO: 1) and said peptide binds to the extracellular domain of ErbB-2. Because the claims encompass methods of targeting therapeutic agents that are nucleic acid constructs, the methods encompass methods of antisense therapy or gene therapy.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The guidance presented in the specification with respect to the targeting of therapeutic agents that are nucleic acid constructs is minimal, because the specification does not provide working examples demonstrating specific methods of therapy where an antisense or gene therapy nucleic acid construct is targeted to a cell or cancer cell, where this targeting results in a therapeutic effect. Because the claims require the use of therapeutic agents, the claims encompass methods intended to have a therapeutic effect. The guidance provided by the specification consists of a discussion of gene therapy vectors on page 31, lines 10-17, and a discussion of antisense mRNA on page 31, line 20 – page 33, line 34.

(A)Antisense

The level of unpredictability in the antisense art is high, as evidenced by the teachings of Shoji (Shoji, Y. and Nakashima, H., Current Pharmaceutical Design, 10: 785-796, 2004), Opalinska (Opalinska, J. and Gewirtz, A.M., Nature Reviews, 1: 503-514, 2002) and Braasch (Braasch, D.A. and Corey, D.R., Biochemistry, 41(14): 4503-4510, 2002). Shoji teaches the problems associated with delivery systems that may be used to deliver antisense molecules, and concludes that further development of delivery systems in vivo without toxicity is required to accomplish more efficient antisense therapy (see page 793, 2nd column). Thus, the problem of delivery of antisense molecules continues to present an obstacle to treatment. Braasch teaches that in vivo trials with antisense compounds have generated initial favorable findings, but also teaches that it is not yet known whether the effects observed are through the intended antisense mechanism (page 4506, 1st column). Braasch also teaches that progress toward the goal of using antisense routinely to inhibit gene expression has been slowed because it is often difficult to predict mRNA sequences that will be susceptible targets for antisense inhibition (see page 4506, 2nd column). Thus, the mechanisms underlying the efficacy of antisense methods is apparently not completely understood and antisense does not appear to be considered a technology that can be routinely used. Opalinska teaches that while nucleic acid mediated gene silencing has been used with great success n the laboratory, and there have been some encouraging results in the clinic, it appears to be widely appreciated that the use antisense in vivo is variable and is not yet a reliable technology (see page 511, 1st column).

In view of the level of unpredictability in the art of in vivo application of antisense technology for the treatment of disease, coupled with the lack of any working examples

providing demonstrating successful targeting in vivo and therapeutic effect for the use of a particular antisense compound in complex with the targeting peptide for the treatment of cancer, one of skill in the art would have to engage in further and undue experimentation. This further experimentation would be undue experimentation because it would encompass experiments in a technology that has not yet become routine for methods of in vivo treatment, and because the mechanisms underlying some of the few clinical success does not appear to be completely understood.

(B)Gene therapy.

The instant specification does not teach how to overcome problems of in vivo delivery and expression nucleic acid constructs as therapeutic agents in gene therapy methods. The state of the art is that in vivo gene delivery is not well developed and is highly unpredictable. For instance Verma (Nature, 1997, Vol. 389, pp. 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression (page 239, column 3). This teaching is repeated in a later publication, Favoro (Favoro, E., et al., Current Opinion Mol. Ther., 9(5): 477-482, 2007; abstract only), which teaches that the problem of delivery has yet to be solved. Additionally, Rubyani (Rubyani, G.M., Molecular Aspects of Medicine, 22: 113-142, 2001) teaches that for successful gene therapy, one must provide therapeutically suitable genes, appropriate delivery systems, and proof of principle. These elements are not provided by the specification with respect to the use of a peptide comprise the sequence KCCYSL to target in vivo nucleic acid constructs to tumors.

The specification does not remedy any of the deficiencies or the prior art with regard to gene therapy. Given the lack of any guidance from the specification on any of the above issues pointed out by Verma, Favoro, or Rubyani, one of skill in the art would be forced to engage in undue experimentation without reasonable expectation of success in order to practice the methods of claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
December 20, 2008
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643